

ANNEX

ANNEX III
LABELLING AND PACKAGE LEAFLET

B. PACKAGE LEAFLET

PACKAGE LEAFLET

TARGRETIN 75 mg Capsules, soft (Bexarotene)

**READ ALL OF THIS LEAFLET CAREFULLY BEFORE YOU START TAKING
THIS MEDICINE.**

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

In this leaflet:

1. What Targretin is and what it is used for
2. Before you take Targretin
3. How to take Targretin
4. Possible side effects
5. Storing Targretin
6. Further Information

Name of medicinal product

Targretin 75 mg Capsules, soft
Bexarotene

Active substance and other ingredients

Targretin is available as soft capsules for oral use in a white plastic bottle containing 100 capsules. Each Targretin capsule contains 75 mg of the active substance bexarotene. The capsules also contain the other ingredients macrogol, polysorbate, povidone and butylated hydroxyanisole.

The capsule shell consists of gelatin, sorbitol special-glycerine blend (glycerin, sorbitol, sorbitol anhydrides (1,4-sorbitan), mannitol and water), titanium dioxide (E171) and printing ink (shellac glaze-45% (20% esterified) in SD-45 alcohol, indigo carmine lake (E132) and simethicone).

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1. WHAT TARGRETIN IS AND WHAT IT IS USED FOR

The active substance in Targretin, bexarotene, belongs to a group of medicines known as retinoids, which are related to vitamin A. Targretin capsules are used by patients with advanced stage cutaneous T-cell lymphoma (CTCL) whose disease has not responded to other therapies. CTCL is a condition in which certain cells of the body's lymph system called T-lymphocytes become cancerous and affect the skin.

2. BEFORE YOU TAKE TARGRETIN

Do not take Targretin:

- if you know that you are allergic to bexarotene or to any of the other ingredients.
- if you are pregnant or breast feeding or if you can become pregnant and are not using effective birth control measures.
- if you have a history of pancreatitis, have uncontrolled lipid (blood fats) elevations (high blood cholesterol or high blood triglycerides), have a condition known as hypervitaminosis A, have uncontrolled thyroid disease, have insufficient liver function or have an ongoing systemic infection.

Take special care with Targretin:

- if you have a known hypersensitivity to retinoids (related to vitamin A), suffer from liver disease, have high blood lipids or take medicines which may cause high blood lipids, have uncontrolled diabetes mellitus (sugar diabetes), have had gall bladder or biliary tract disease, or consume excessive amounts of alcohol. If any of these apply you should inform your doctor.

Your fasting blood lipid determinations may have to be performed before therapy is initiated and at weekly intervals afterwards, and then monthly while taking this medicine.

Blood tests to evaluate the function of your liver and thyroid gland and to monitor your red blood cell and white blood cell counts will be obtained before therapy is started and will be monitored during therapy.

Periodic eye exams may be needed if you experience visual difficulties while taking this medicine.

Minimise exposure to sunlight as much as possible and avoid exposure to sun lamps.

Do not take more than 15,000 International Units of vitamin A supplements per day during treatment.

Targretin capsules should not be used in children or adolescents.

Taking Targretin with food and drink:

Targretin should be taken with food. If you regularly consume grapefruit or grapefruit juice, please consult your doctor as these have the potential to alter your body's response to Targretin therapy.

Pregnancy or breast-feeding:

Targretin may be harmful to a developing foetus. DO NOT use Targretin if you are pregnant or breast-feeding. If you are pregnant, thinking of becoming pregnant, or breast-feeding, ask your doctor for more information. If you are capable of becoming pregnant, you must have a pregnancy test within one week before you start therapy, confirming you are not pregnant. You must use effective contraception (birth control) continuously starting one month before

beginning therapy until one month after you stop taking Targretin. It is recommended that two reliable forms of contraception be used together. If you are taking a hormonal contraceptive (for example, birth control pills), you should discuss this with your doctor.

If you are male and your partner is pregnant or capable of becoming pregnant, you must use condoms during sexual intercourse while taking bexarotene and for at least one month after the last dose.

Driving and using machines:

It is not known whether Targretin has an effect on your ability to drive a car or operate machinery. If you experience dizziness or problems with your vision during therapy, do not drive or operate machinery.

Important information about some of the ingredients of Targretin:

Butylated hydroxyanisol, an ingredient in Targretin, is an irritant to the eyes, skin, and mucous membranes, therefore the capsules must be swallowed intact.

Taking other medicines:

Before starting treatment, make sure your doctor knows if you are taking medicines (including those not prescribed by your doctor), such as ketoconazole and itraconazole (used against fungal infections), erythromycin, clarithromycin and rifampicin (used against bacterial infections), phenytoin and phenobarbital (used against seizures), gemfibrozil (used to reduce high levels of fats in the blood such as triglycerides and cholesterol), vitamin A supplements, protease inhibitors (used against viral infections), tamoxifen (used against some forms of cancer) or dexamethasone (used for inflammatory conditions). This is important as using more than one medicine at the same time can strengthen or weaken the effect of the medicines.

3. HOW TO TAKE TARGRETIN

Always take Targretin exactly as your doctor tells you to. The doctor will prescribe a suitable dose for you, which is generally 4 to 10 capsules to be taken once daily. Take your prescribed number of capsules at the same time each day with a meal. The capsules can be taken immediately before, during or immediately after the course of the meal, if preferred. The capsules should be swallowed whole and not chewed.

How long you should take Targretin:

Do not stop taking your medication until your doctor advises you to do so. Although some patients have improvement within the first several weeks, most patients require several months or more of treatment to improve.

If you take more Targretin than you should:

If you have taken more than the prescribed dose of Targretin, you must contact your doctor.

If you forget to take Targretin:

If you forget to take one dose, take your daily dose with your next meal on the same day, then take your usual dose as normal, the following day. Do not take a double dose in one day to make up for a missed dose the previous day.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Targretin can have side effects. Tell your doctor as soon as possible if you feel any deterioration in your condition while you are taking Targretin. Sometimes it is necessary to adjust the dose or interrupt treatment. Your doctor will advise you on what to do.

The following side effects were reported in patients with CTCL who were treated with the recommended initial dose of capsules.

Very common:

Low white blood cell count
lowering of thyroid hormones level
Elevation of blood fats (triglycerides and cholesterol)
Skin reactions (Itching, redness, irritation, peeling)
Headache, fatigue, pain

Common:

Low red blood cell count, enlarged lymph nodes, worsening of lymphoma
Thyroid disorder
Elevation of liver enzymes, impaired kidney function, low protein in blood, weight gain
Insomnia, dizziness, reduced skin sensation
Dry eyes, deafness, abnormal sensations of the eye including irritation and heaviness
Swelling of legs and arms
Nausea, diarrhoea, dry mouth, dry lips, loss of appetite, constipation, excess gas, abnormal liver function tests, vomiting
Dry skin, skin disorder, loss of hair, skin ulcer, acne, skin thickening, skin nodule, increased sweating
Joint aches, bone pain, muscle aches
Chills, abdominal pain, allergic reaction, infection

Uncommon:

Blood disorders, eosinophilia, leukocytosis, lymphocytosis, purpura, elevated and decreased numbers of blood platelets
Overactive thyroid
Elevated bilirubin in the blood, impaired kidney function, gout, decreased HDL cholesterol
Agitation, difficulties with balance, depression, increased skin sensation on touching, abnormal nerve sensations, vertigo
Abnormal vision, blurred vision, inflammation of the eye lids, cataract, inflammation of the white part of the eye, lesion of the cornea of the eye, ear disorder, defect in field of vision
Swelling, bleeding, high blood pressure, fast heart rate, visible vein enlargement, dilation of blood vessels
Gastrointestinal disorder, liver failure, inflammation of the pancreas
Changes in hair, herpes simplex, nail disorder, pustular rash, serous drainage, skin discoloration
Muscle weakness
Proteins in urine, abnormal kidney function
Back pain, skin infection, fever, parasitic infection, abnormal laboratory test, disorder of mucous membrane, tumour

Rare fatal side effects are acute inflammation of the pancreas, bleeding in the head, and liver failure.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. STORING TARGRETIN

Always keep this medicine in the closed original pack and out of the reach and sight of children.

Do not store above 30°C. Keep the bottle tightly closed.

Always ensure the container is tightly closed after each dose is removed and store in a dry place.

Do not use after the expiry date stated on the package.

6. FURTHER INFORMATION

For any information about this medicinal product please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last approved on